WEST Search History

DATE: Friday, December 05, 2003

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=OR			
L6	L5 and DNA	32	L6
L5	L4 and fragment	33	L5
L4	L3 and mutate?	35	L4
L3	L2 and LF	89	L3
L2	L1 and PA	674	L2
L1	Anthrax	1869	L1

END OF SEARCH HISTORY

updated search

09/747,521

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Terms	Documents
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Search Results - Record(s) 31 through 32 of 32 returned.

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☐ 32. 5591631 . 12 Feb 93; 07 Jan 97. Anthrax toxin fusion proteins, nucleic acid encoding same. Leppla; Stephen H., et al. 435/252.3; 435/320.1 530/350 530/402 536/23.4 536/23.7. C07K019/00 C12N015/31 C12N015/70.

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L6: Entry 31 of 32 File: USPT Oct 14, 1997

US-PAT-NO: 5677274
DOCUMENT-IDENTIFIER: US 5677274 A
**** See image for Certificate of Correction ****

TITLE: Anthrax toxin fusion proteins and related methods

DATE-ISSUED: October 14, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Leppla; Stephen H.	Bethesda	MD		
Klimpel; Kurt R.	Gaithersburg	MD		
Arora; Naveen	Delhi			IN
Singh; Yogendra	Delhi			IN
Nichols; Peter J.	Welling Kent			GB

US-CL-CURRENT: 514/2

CLAIMS:

We claim:

1. A method for targeting compounds having a desired biological activity not present on native anthrax lethal factor (LF) to a specific cell population, comprising:

a) administering to the cell population a first compound comprising a first protein consisting essentially of:

i) the translocation domain and the anthrax lethal factor (LF) binding domain of the native anthrax protective antigen (PA) protein, and

ii) a ligand domain that specifically binds the first protein to a target on the surface of the cell population to bind the first compound to said surface; and

b) administering to the resultant cell population a second compound comprising a fusion protein or conjugate consisting essentially of:

i) the anthrax protective antigen (PA) binding domain of the native anthrax lethal factor (LF) protein, chemically attached to

ii) a biological activity-inducing polypeptide to bind the second compound to the first compound on the surface of the cell population, internalize the second compound into the cell population, and effect the activity of the polypeptide therein.

2. A method according to claim 1, wherein the anthrax protective antigen (PA) binding domain of said second compound comprises at least the first 254 amino acid residues but less than all of the amino acid residues of the anthrax lethal factor (SEQ. ID NO: 2).

3. A method according to claim 1, wherein the ligand domain of said first compound is the ligand domain of the native anthrax protective antigen (PA)

protein.

4. A method according to claim 1, wherein said second compound comprises the anthrax protective antigen (PA) binding domain of the native anthrax lethal factor (LF) protein chemically attached to a polypeptide through a peptide bond.

5. The method of claim 1, wherein the polypeptide of said second compound is a toxin.

6. The method of claim 1, wherein the polypeptide of said second compound is an enzyme.

7. The method of claim 1, wherein the ligand domain of said first compound is an antibody.

8. The method of claim 1, wherein the ligand domain of said first compound is a growth factor.

9. The method of claim 5, wherein the polypeptide of said second compound is Pseudomonas exotoxin A (PE).

10. The method of claim 5, wherein the polypeptide of said second compound is the A chain of Diptheria toxin.

11. The method of claim 5, wherein the polypeptide of said second compound is shiga toxin.

12. The method of claim 7, wherein the ligand domain of said first compound is a single chain antibody.

End of Result Set

Generate Collection

L6: Entry 32 of 32 File: USPT Jan 7, 1997

US-PAT-NO: 5591631
DOCUMENT-IDENTIFIER: US 5591631 A

TITLE: Anthrax toxin fusion proteins, nucleic acid encoding same

DATE-ISSUED: January 7, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Leppla; Stephen H.	Bethesda	MD		
Klimpel; Kurt R.	Gaithersburg	MD		
Arora; Naveen	Delhi			IN
Singh; Yogendra	Delhi			IN
Nicholls; Peter J.	Welling Kent			GB

US-CL-CURRENT: 435/252.3; 435/320.1, 530/350, 530/402, 536/23.4, 536/23.7

CLAIMS:

What is claimed is:

1. A nucleic acid encoding a fusion protein, comprising a nucleotide sequence encoding the protective antigen (PA) binding domain of the native lethal factor (LF) protein and a nucleotide sequence encoding a polypeptide, wherein said fusion protein lacks the catalytic domain of LF.

2. The nucleic acid of claim 1, wherein the polypeptide is a toxin.

3. The nucleic acid of claim 2, wherein the toxin is Pseudomonas exotoxin A.

4. The nucleic acid of claim 2, wherein the toxin is the A chain of Diphtheria toxin.

5. The nucleic acid of claim 2, wherein the toxin is shiga toxin.

6. The nucleic acid of claim 1, comprising the nucleotide sequence defined in the Sequence Listing as SEQ ID NO:5.

7. The nucleic acid of claim 1, wherein the fusion protein comprises the protein defined in the Sequence Listing as SEQ ID NO:6.

8. A protein encoded by the nucleic acid of claim 1.

9. A vector comprising the nucleic acid of claim 1.

10. The vector of claim 9 in a host that expresses the protein encoded by the nucleic acid.

11. A compound comprising the protective antigen (PA) binding domain of the native lethal factor (LF) protein chemically attached to a polypeptide, wherein said compound lacks the catalytic domain of LF.

12. The compound of claim 11 wherein the polypeptide is a toxin.

13. The compound of claim 11 wherein the polypeptide is a growth factor.

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L6: Entry 8 of 32 File: PGPB Oct 23, 2003

PGPUB-DOCUMENT-NUMBER: 20030198651
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030198651 A1

TITLE: Targeting antigens to the MHC class I processing pathway with an anthrax toxin fusion protein

PUBLICATION-DATE: October 23, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Klimpel, Kurt	Gaithersburg	MD	US	
Goletz, Theresa J.	Kensington	MD	US	
Arora, Naveen	Delhi	MD	IN	
Leppla, Stephen H.	Bethesda	MD	US	
Berzofsky, Jay A.	Bethesda		US	

ASSIGNEE-INFORMATION:

NAME	CITY	STATE	COUNTRY	TYPE CODE
Government of the USA as represented by the Secretary of the Dept of Health and Human Services	Rockville	MD		02

APPL-NO: 10/ 446890 [PALM]
DATE FILED: May 27, 2003

RELATED-US-APPL-DATA:
Application 10/446890 is a division-of US application 08/937276, filed September 15, 1997, US Patent No. 6592872
Application is a non-provisional-of-provisional application 60/025270, filed September 17, 1996,

INT-CL: [07] A61 K 39/07

US-CL-PUBLISHED: 424/246.1
US-CL-CURRENT: 424/246.1

ABSTRACT:

The present invention provides a vaccine for inducing an immune response in mammal to a specific antigen, where the vaccine comprises a unit dose of a binary toxin protective antigen and the antigen, which is bound to a binary toxin protective antigen binding protein. In one embodiment the vaccine is comprised of an anthrax protective antigen and the antigen bound to anthrax protective antigen binding protein. The present invention also provides a method of immunizing a mammal against an antigen using the vaccine, and a method of inducing antigen-presenting mammalian cells to present specific antigens via the MHC class I processing pathway.

CROSS REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of provisional application 60/025,270, filed Sep. 17, 1996.

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L6: Entry 8 of 32 File: PGPB Oct 23, 2003

PGPUB-DOCUMENT-NUMBER: 20030198651
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030198651 A1

TITLE: Targeting antigens to the MHC class I processing pathway with an anthrax toxin fusion protein

PUBLICATION-DATE: October 23, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Klimpel, Kurt	Gaithersburg	MD	US	
Goletz, Theresa J.	Kensington	MD	US	
Arora, Naveen	Delhi	MD	IN	
Leppla, Stephen H.	Bethesda	MD	US	
Berzofsky, Jay A.	Bethesda		US	

US-CL-CURRENT: 424/246.1

CLAIMS:

What is claimed is:

1. A vaccine capable of inducing an immune response in a mammal to a specific antigen wherein the vaccine comprises a unit dose of an anthrax protective antigen and said specific antigen bound to an anthrax protective antigen binding protein.

2. The vaccine of claim 1 wherein the protective antigen is a processed protective antigen.

3. The vaccine of claim 1 wherein the vaccine is sterile.

4. The vaccine of claim 1 wherein the vaccine further comprises physiologically compatible salts.

5. The vaccine of claim 4 wherein the vaccine is in an aqueous solution of physiologically compatible salts.

6. The vaccine of claim 1 wherein the anthrax protective antigen binding protein is the lethal factor of Bacillus anthracis.

7. The vaccine of claim 1 wherein the anthrax protective antigen binding protein comprises at least about the first 250 amino acid residues of the lethal factor of Bacillus anthracis and less than all of the amino acid residues of the lethal factor.

8. The vaccine of claim 1 wherein the molar ratio of protective antigen to the antigen bound to an anthrax protective antigen binding protein is greater than one.

9. A method of immunizing a mammal against an antigen which comprises administering a safe and effective amount of a vaccine comprising an anthrax protective antigen and said antigen bound to an anthrax protective antigen binding protein.

10. The method of claim 9 wherein the protective antigen is a processed protective antigen.

11. The method of claim 9 wherein the vaccine is sterile.

12. The method of claim 9 wherein the vaccine further comprises physiologically

compatible salts.

13. The method of claim 12 wherein the vaccine is in an aqueous solution of physiologically compatible salts.

14. The method of claim 9 wherein the anthrax protective antigen binding protein is the lethal factor of Bacillus anthracis.

15. The method of claim 9 wherein the anthrax protective antigen binding protein comprises at least about the first 250 amino acid residues of the lethal factor of Bacillus anthracis and less than all of the amino acid residues of the lethal factor.

16. The method of claim 9 wherein the molar ratio of protective antigen to the antigen bound to an anthrax protective antigen binding protein is greater than one.

17. The method of claim 9 wherein the vaccine is administered via parenteral injection.

18. The method of claim 9 wherein the vaccine is administered via subcutaneous injection.

19. The method of claim 9 wherein the vaccine is administered in a unit dose that is between 10 to 500 nanograms of antigen bound to an anthrax protective antigen binding protein per kilogram of said mammal.

20. A method of inducing antigen presenting mammalian cells to present specific antigens on their cell membranes via the MHC class I processing pathway, comprising: i) selecting cells that can process and present specific antigens on their cell membranes via the MHC class I processing pathway; ii) contacting the cells with an anthrax protective antigen and said specific antigen bound to an anthrax protective antigen binding protein; and, iii) permitting the cells to internalize, process and present said specific antigen bound to an anthrax protective antigen binding protein on its cell membrane, forming a specific antigen presenting cell.

21. A method of claim 20 wherein the antigen presenting mammalian cells are further contacted with an effector lymphocyte cell that recognizes the antigen presented on the cell membranes of the antigen presenting cells.

22. The method of claim 20 wherein the protective antigen is a processed protective antigen.

23. The method of claim 20 wherein the anthrax protective antigen binding protein is the lethal factor of Bacillus anthracis.

24. The method of claim 20 wherein the anthrax protective antigen binding protein comprises at least about the first 250 amino acid residues of the lethal factor of Bacillus anthracis and less than all of the amino acid residues of the lethal factor.

25. The method of claim 20 wherein the molar ratio of protective antigen to the antigen bound to an anthrax protective antigen binding protein is greater than one.

26. The method of claim 20 where said antigen presenting cell is a dendritic cell.

27. A vaccine for inducing an immune response in a mammal to a specific antigen wherein the vaccine comprises a unit dose of a binary toxin protective antigen and the antigen bound to a binary toxin protective antigen binding protein wherein the binary toxin is selected from the group comprising iota toxin and anthrax toxin.

28. The vaccine of claim 27, wherein the binary toxin is iota toxin.

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L6: Entry 15 of 32 File: PGPB May 22, 2003

PGPUB-DOCUMENT-NUMBER: 20030096333
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030096333 A1

TITLE: Anthrax lethal factor is a MAPK kinase protease

PUBLICATION-DATE: May 22, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Duesbery, Nicholas	Grand Rapids	MI	US	
Webb, Craig	Rockford	MI	US	
Leppla, Stephen	Bethesda	MD	US	
Vande Woude, George	Ada	MI	US	

US-CL-CURRENT: 435/15; 435/7.23, 702/19

CLAIMS:

What is claimed is:

1. An in vitro method for screening modulators of lethal factor (LF) mitogen activated protein kinase kinase (MAPKK) protease activity, the method comprising the steps of: (i) providing LF in an aqueous solution, wherein the LF has MAPKK protease activity in the solution; (ii) contacting LF with substances suspected of having the ability to modulate MAPKK protease activity; and (iii) assaying for the level of LF MAPKK protease activity.

2. The method of claim 1, wherein the LF is recombinant.

3. The method of claim 1, wherein the step of assaying comprises a Mos-induced activation of MAPK assay in a Xenopus oocyte lysate.

4. The method of claim 1, wherein the step of assaying comprises an MAPKK1 or MAPKK2 mobility assay.

5. The method of claim 4, wherein the MAPKK1 or MAPKK2 is recombinant.

6. The method of claim 5, wherein the recombinant MAPKK1 or recombinant MAPKK2 is linked to a detectable moiety.

7. The method of claim 1, wherein the step of assaying comprises an myelin basic protein (MBP) phosphorylation assay.

8. A kit for screening in vitro for modulators of lethal factor (LF) mitogen activated protein kinase kinase (MAPKK) protease activity, the kit comprising; (i) a container holding LF, wherein the LF has MAPKK protease activity; and (ii) instructions for assaying for LF MAPKK protease activity.

9. A kit of claim 8, wherein the LF is recombinant.

10. A in vivo method for screening modulators of lethal factor (LF) mitogen activated protein kinase kinase (MAPKK) protease activity, the method comprising the steps of: (i) contacting a living cell with LF, wherein the LF has MAPKK protease activity; (ii) contacting the cell with substances suspected of having the ability to modulate MAPKK protease activity; and (iii) assaying for the level of LF MAPKK protease activity.

11. The method of claim 10, wherein the LF is recombinant.

12. The method of claim 10, wherein the step of contacting the cell comprises transducing the cell with an expression vector encoding LF.

13. The method of claim 10, wherein the step of contacting further comprises contacting a cell with LF in the presence of protective antigen (PA).

14. The method of claim 10, wherein the mitogen activated protein kinase (MAPK) signal transduction pathway is activated in the cell.

15. The method of claim 10, wherein the cell is a human cell.

16. The method of claim 10, wherein the cell is a Xenopus oocyte.

17. The method of claim 10, wherein the cell is a cancer cell.

18. The method of claim 17, wherein the cancer cell is from a sarcoma.

19. The method of claim 10, wherein the cell is from a transformed cell line.

20. The method of claim 19, wherein the cell line is transformed with Ras.

21. The method of claim 10, wherein the step of assaying comprises an MAPKK1 or MAPKK2 mobility assay.

22. The method of claim 10, wherein the step of assaying comprises a Mos-induced activation of MAPK assay in a Xenopus oocyte.

23. The method of claim 10, wherein the MAPKK1 or MAPKK2 is recombinant.

24. The method of claim 23, wherein the recombinant MAPKK1 or recombinant MAPKK2 is linked to a detectable moiety.

25. An in vitro method for screening mimetics of lethal factor (LF) having mitogen activated protein kinase kinase (MAPKK) protease activity, the method comprising the steps of: (i) providing a compound suspected of being an LF mimetic in an aqueous solution; and (ii) assaying for the level of MAPKK protease activity.

26. The method of claim 25, wherein the step of assaying comprises a Mos-induced activation of MAPK assay in a Xenopus oocyte lysate.

27. The method of claim 25, wherein the step of assaying comprises an MAPKK1 or MAPKK2 mobility assay.

28. The method of claim 27, wherein the MAPKK1 or MAPKK2 is recombinant.

29. The method of claim 28, wherein the recombinant MAPKK1 or recombinant MAPKK2 is linked to a detectable moiety.

30. The method of claim 25, wherein the step of assaying comprises an myelin basic protein (MBP) phosphorylation assay.

31. An in vivo method for screening mimetics of lethal factor (LF) having mitogen activated protein kinase kinase (MAPKK) protease activity, the method comprising the steps of: (i) contacting a living cell with a compound suspected of being an LF mimetic; and (ii) assaying for the level of MAPKK protease activity.

32. The method of claim 31, wherein the mitogen activated protein kinase (MAPK) signal transduction pathway is activated in the cell.

33. The method of claim 31, wherein the cell is a human cell.

34. The method of claim 31, wherein the cell is a Xenopus oocyte.

35. The method of claim 31, wherein the cell is a cancer cell.

36. The method of claim 35, wherein the cancer cell is from a sarcoma.

37. The method of claim 31, wherein the cell is from a transformed cell line.

38. The method of claim 37, wherein the cell line is transformed with Ras.

39. The method of claim 31, wherein the step of assaying comprises an MAPKK1 or MAPKK2 mobility assay.

40. The method of claim 31, wherein the step of assaying comprises a Mos-induced activation of MAPK assay in a Xenopus oocyte.

41. The method of claim 31, wherein the MAPKK1 or MAPKK2 is recombinant.

42. A method for inhibiting proliferation of a cancer cell, the method comprising the step of contacting the cell with LF, wherein the LF has MAPKK protease activity.

43. The method of claim 42, wherein the LF is recombinant.

44. The method of claim 42, wherein the step of contacting the cell comprises transducing the cell with an expression vector encoding LF.

45. The method of claim 42, wherein the step of contacting further comprises contacting a cell with LF in the presence of protective antigen (PA).

46. The method of claim 45, wherein the PA is a fusion protein targeted to the cancer cell.

47. The method of claim 42, wherein the mitogen activated protein kinase (MAPK) signal transduction pathway is activated in the cancer cell.

48. The method of claim 42, wherein the cell is a human cell.

49. The method of claim 42, wherein the cancer cell is from a sarcoma.

50. The method of claim 42, wherein the cell is from a transformed cell line.

51. The method of claim 50, wherein the cell line is transformed with Ras.

52. In a computer system, a method for identifying a three-dimensional structure of LF proteins, the method comprising the steps of: (i) receiving input of at least 10 contiguous amino acids of the amino acid sequence of LF or at least 30 contiguous nucleotides of the nucleotide sequence of a gene encoding LF, and conservatively modified variants thereof; and (ii) generating a three-dimensional structure of the protein encoded by the amino acid sequence.

53. The method of claim 52, wherein said amino acid sequence is a primary structure and wherein said generating step includes the steps of: (i) forming a secondary structure from said primary structure using energy terms encoded by the primary structure; and (ii) forming a tertiary structure from said secondary structure using energy terms encoded by said secondary structure.

54. The method of claim 52, wherein said generating step includes the step of forming a quaternary structure from said tertiary structure using anisotropic terms encoded by the tertiary structure.

55. The method of claim 53, wherein said generating step further includes the step of forming a quaternary structure from said tertiary structure using anisotropic terms encoded by the tertiary structure.

56. The method of claim 52, further comprising the step of identifying regions of the three-dimensional structure of the protein that bind to ligands and using the regions to identify ligands that bind to the protein.

57. In a computer system, a method for identifying a three-dimensional structure of MAPKK proteins, the method comprising the steps of: (i) receiving input of at least 10 contiguous amino acids of the amino acid sequence of MAPKK or at least 30 contiguous nucleotides of the nucleotide sequence of a gene encoding MAPKK, and conservatively modified variants thereof; and (ii) generating a three-dimensional structure of the protein encoded by the amino acid sequence.

58. The method of claim 57, wherein said amino acid sequence is a primary structure and wherein said generating step includes the steps of: (i) forming a secondary structure

from said primary structure using energy terms encoded by the primary structure; and (ii) forming a tertiary structure from said secondary structure using energy terms encoded by said secondary structure.

59. The method of claim 57, wherein said generating step includes the step of forming a quaternary structure from said tertiary structure using anisotropic terms encoded by the tertiary structure.

60. The method of claim 58, wherein said generating step further includes the step of forming a quaternary structure from said tertiary structure using anisotropic terms encoded by the tertiary structure.

61. The method of claim 57, further comprising the step of identifying regions of the three-dimensional structure of the protein that bind to ligands and using the regions to identify ligands that bind to the protein.

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TITLE: Anthrax lethal factor is a MAPK kinase protease

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CLAIMS:

What is claimed is:

1. An in vitro method for screening modulators of lethal factor (LF) mitogen activated protein kinase kinase (MAPKK) protease activity, the method comprising the steps of: (i) providing LF in an aqueous solution, wherein the LF has MAPKK protease activity in the solution; (ii) contacting LF with substances suspected of having the ability to modulate MAPKK protease activity; and (iii) assaying for the level of LF MAPKK protease activity.

2. The method of claim 1, wherein the LF is recombinant.

3. The method of claim 1, wherein the step of assaying comprises a Mos-induced activation of MAPK assay in a Xenopus oocyte lysate.

4. The method of claim 1, wherein the step of assaying comprises an MAPKK1 or MAPKK2 mobility assay.

5. The method of claim 4, wherein the MAPKK1 or MAPKK2 is recombinant.

6. The method of claim 5, wherein the recombinant MAPKK1 or recombinant MAPKK2 is linked to a detectable moiety.

7. The method of claim 1, wherein the step of assaying comprises an myelin basic protein (MBP) phosphorylation assay.

8. A kit for screening in vitro for modulators of lethal factor (LF) mitogen activated protein kinase kinase (MAPKK) protease activity, the kit comprising; (i) a container holding LF, wherein the LF has MAPKK protease activity; and (ii) instructions for assaying for LF MAPKK protease activity.

9. A kit of claim 8, wherein the LF is recombinant.

10. A in vivo method for screening modulators of lethal factor (LF) mitogen activated protein kinase kinase (MAPKK) protease activity, the method comprising the steps of: (i) contacting a living cell with LF, wherein the LF has MAPKK protease activity; (ii) contacting the cell with substances suspected of having the ability to modulate MAPKK protease activity; and (iii) assaying for the level of LF MAPKK protease activity.

11. The method of claim 10, wherein the LF is recombinant.

12. The method of claim 10, wherein the step of contacting the cell comprises transducing the cell with an expression vector encoding LF.

13. The method of claim 10, wherein the step of contacting further comprises contacting a cell with LF in the presence of protective antigen (PA).

14. The method of claim 10, wherein the mitogen activated protein kinase (MAPK) signal transduction pathway is activated in the cell.

15. The method of claim 10, wherein the cell is a human cell.

16. The method of claim 10, wherein the cell is a Xenopus oocyte.

17. The method of claim 10, wherein the cell is a cancer cell.

18. The method of claim 17, wherein the cancer cell is from a sarcoma.

19. The method of claim 10, wherein the cell is from a transformed cell line.

20. The method of claim 19, wherein the cell line is transformed with Ras.

21. The method of claim 10, wherein the step of assaying comprises an MAPKK1 or MAPKK2 mobility assay.

22. The method of claim 10, wherein the step of assaying comprises a Mos-induced activation of MAPK assay in a Xenopus oocyte.

23. The method of claim 10, wherein the MAPKK1 or MAPKK2 is recombinant.

24. The method of claim 23, wherein the recombinant MAPKK1 or recombinant MAPKK2 is linked to a detectable moiety.

25. An in vitro method for screening mimetics of lethal factor (LF) having mitogen activated protein kinase kinase (MAPKK) protease activity, the method comprising the steps of: (i) providing a compound suspected of being an LF mimetic in an aqueous solution; and (ii) assaying for the level of MAPKK protease activity.

26. The method of claim 25, wherein the step of assaying comprises a Mos-induced activation of MAPK assay in a Xenopus oocyte lysate.

27. The method of claim 25, wherein the step of assaying comprises an MAPKK1 or MAPKK2 mobility assay.

28. The method of claim 27, wherein the MAPKK1 or MAPKK2 is recombinant.

29. The method of claim 28, wherein the recombinant MAPKK1 or recombinant MAPKK2 is linked to a detectable moiety.

30. The method of claim 25, wherein the step of assaying comprises an myelin basic protein (MBP) phosphorylation assay.

31. An in vivo method for screening mimetics of lethal factor (LF) having mitogen activated protein kinase kinase (MAPKK) protease activity, the method comprising the steps of: (i) contacting a living cell with a compound suspected of being an LF mimetic; and (ii) assaying for the level of MAPKK protease activity.

32. The method of claim 31, wherein the mitogen activated protein kinase (MAPK) signal transduction pathway is activated in the cell.

33. The method of claim 31, wherein the cell is a human cell.

34. The method of claim 31, wherein the cell is a Xenopus oocyte.

35. The method of claim 31, wherein the cell is a cancer cell.

36. The method of claim 35, wherein the cancer cell is from a sarcoma.

37. The method of claim 31, wherein the cell is from a transformed cell line.

38. The method of claim 37, wherein the cell line is transformed with Ras.

39. The method of claim 31, wherein the step of assaying comprises an MAPKK1 or MAPKK2 mobility assay.

40. The method of claim 31, wherein the step of assaying comprises a Mos-induced activation of MAPK assay in a Xenopus oocyte.

41. The method of claim 31, wherein the MAPKK1 or MAPKK2 is recombinant.

42. A method for inhibiting proliferation of a cancer cell, the method comprising the step of contacting the cell with LF, wherein the LF has MAPKK protease activity.

43. The method of claim 42, wherein the LF is recombinant.

44. The method of claim 42, wherein the step of contacting the cell comprises transducing the cell with an expression vector encoding LF.

45. The method of claim 42, wherein the step of contacting further comprises contacting a cell with LF in the presence of protective antigen (PA).

46. The method of claim 45, wherein the PA is a fusion protein targeted to the cancer cell.

47. The method of claim 42, wherein the mitogen activated protein kinase (MAPK) signal transduction pathway is activated in the cancer cell.

48. The method of claim 42, wherein the cell is a human cell.

49. The method of claim 42, wherein the cancer cell is from a sarcoma.

50. The method of claim 42, wherein the cell is from a transformed cell line.

51. The method of claim 50, wherein the cell line is transformed with Ras.

52. In a computer system, a method for identifying a three-dimensional structure of LF proteins, the method comprising the steps of: (i) receiving input of at least 10 contiguous amino acids of the amino acid sequence of LF or at least 30 contiguous nucleotides of the nucleotide sequence of a gene encoding LF, and conservatively modified variants thereof; and (ii) generating a three-dimensional structure of the protein encoded by the amino acid sequence.

53. The method of claim 52, wherein said amino acid sequence is a primary structure and wherein said generating step includes the steps of: (i) forming a secondary structure from said primary structure using energy terms encoded by the primary structure; and (ii) forming a tertiary structure from said secondary structure using energy terms encoded by said secondary structure.

54. The method of claim 52, wherein said generating step includes the step of forming a quaternary structure from said tertiary structure using anisotropic terms encoded by the tertiary structure.

55. The method of claim 53, wherein said generating step further includes the step of forming a quaternary structure from said tertiary structure using anisotropic terms encoded by the tertiary structure.

56. The method of claim 52, further comprising the step of identifying regions of the three-dimensional structure of the protein that bind to ligands and using the regions to identify ligands that bind to the protein.

57. In a computer system, a method for identifying a three-dimensional structure of MAPKK proteins, the method comprising the steps of: (i) receiving input of at least 10 contiguous amino acids of the amino acid sequence of MAPKK or at least 30 contiguous nucleotides of the nucleotide sequence of a gene encoding MAPKK, and conservatively modified variants thereof; and (ii) generating a three-dimensional structure of the protein encoded by the amino acid sequence.

58. The method of claim 57, wherein said amino acid sequence is a primary structure and wherein said generating step includes the steps of: (i) forming a secondary structure

from said primary structure using energy terms encoded by the primary structure; and (ii) forming a tertiary structure from said secondary structure using energy terms encoded by said secondary structure.

59. The method of claim 57, wherein said generating step includes the step of forming a quaternary structure from said tertiary structure using anisotropic terms encoded by the tertiary structure.

60. The method of claim 58, wherein said generating step further includes the step of forming a quaternary structure from said tertiary structure using anisotropic terms encoded by the tertiary structure.

61. The method of claim 57, further comprising the step of identifying regions of the three-dimensional structure of the protein that bind to ligands and using the regions to identify ligands that bind to the protein.